UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte GERALD R. CRABTREE, ISABELLA GRAEF,
and FENG CHEN

Appeal 2007-1040
Application 09/960,708
Technology Center 1600

Decided: May 29, 2007

Before DONALD E. ADAMS, DEMETRA J. MILLS, and
ERIC GRIMES, *Administrative Patent Judges*.

ADAMS, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal involves claims 8-11, 15-18, 35-44, 46, and 47, the only claims pending in this application. We have jurisdiction over the appeal pursuant to 35 U.S.C. § 134.

INTRODUCTION

The claims are directed toward methods of inhibiting (a) angiogenesis/vascular development in a host (claims 8 and 46) or (b) tumor growth in a host (claims 15 and 47). The methods of claims 8 and 15 comprise the single step of *systemically administering* an effective amount of a *Ca2+/calcineurin/NF-ATc inhibitory agent* to the host. The methods of claims 46 and 47 comprise the single step of *administering* an effective amount of *a cyclosporin* to the host. Claims 8, 15, 46, and 47 are reproduced below:

8. A method of inhibiting angiogenesis/vascular development in a host having a condition associated with unwanted angiogenesis, said method comprising:

systemically administering to said host an effective amount of a Ca2+/calcineurin/NF-ATc inhibitory agent to inhibit angiogenesis/vascular development in said host having a condition associated with unwanted angiogenesis.

15. A method of inhibiting tumor growth in a host having a neoplastic disease condition, said method comprising:

systemically administering to said host having a neoplastic disease condition an

effective amount of a Ca2+/calcineurin/NF-ATc inhibitory agent to inhibit tumor growth in said host.

46. A method of inhibiting angiogenesis/vascular development in a host having a condition associated with unwanted angiogenesis, said method comprising:

administering to said host an effective amount of a cyclosporin to inhibit angiogenesis/vascular development in a host having a condition associated with unwanted angiogenesis.

47. A method of inhibiting tumor growth in a host having a neoplastic disease condition, said method comprising:

administering to said host an effective amount of a cyclosporin to inhibit tumor growth in said host having a neoplastic disease condition.

The Examiner relies on the following prior art references to show unpatentability:

Flanagan et al. (Flanagan), "Nuclear association of a T-cell transcription factor blocked by FK-506 and cyclosporin A," Nature, Vol. 352, pp. 803-807 (1991).

Jiang et al. (Jiang), "Anti-tumor-promoting action of FK506, a potent immunosuppressive agent," Carcinogenesis, Vol. 14, pp. 67-71 (1993).

Bolontrade et al. (Bolontrade), "Angiogenesis is an early event in the development of chemically induced skin tumors," Carcinogenesis, Vol. 19(12), pp. 2107-2133 (1998).

The rejections as presented by the Examiner are as follows:

1. Claims 8-11, 15-18, 35, 37, 39, 40, and 44 stand rejected under 35 U.S.C. § 102(b) as anticipated by Jiang.

2. Claims 36-44, 46, and 47 stand rejected under 35 U.S.C. § 103 as being unpatentable over the combination of Jiang and Flanagan.

We reverse the rejection under 35 U.S.C. § 102(b) and the rejection of claims 36-44 under 35 U.S.C. § 103. We affirm the rejection of claims 46 and 47 under 35 U.S.C. § 103.

FINDINGS OF FACT

1. A Ca2+/calcineurin/NF-ATc inhibitory agent includes FK506, rapamycin, and cyclosporin A [(CsA)] (Specification 6: ¶ 20).

2. FK506 and CsA are immunosuppressive agents (Jiang 67, col. 1, ll. 1-5).

3. The term "effective amount" means "the amount required to achieve the desired result . . . where such amounts may readily be determined empirically"[1] (Specification 8: ¶ 24).

4. The active "agent may be administered to the host using any convenient means capable of producing the desired result" (Specification 8: ¶ 25). We understand this to mean that the agent can be administered both topically and systemically.

5. The term "inhibiting" means "prevented from happening, or stopped" (Specification 11: ¶ 34).

6. The term "host" encompasses "rodentia (e.g., mice, guinea pigs, and rats) . . . " (Specification 11: ¶ 35).

7. "[S]ystemic administration of immunosuppressants promotes carcinogenesis in parallel with the suppression of T cell functions" (Jiang 69, col. 2, ll. 49-51).

8. "In contrast to the case of systemic administration, topical application of CsA . . . markedly suppressed skin tumor promotion caused by TPA . . ." (Jiang 69, col. 2, ll. 12-20).

9. Jiang teaches "the inhibition of tumor formation in mice comprising the [topical] administration of FK506" (Answer 3; Br. 7).

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[1] According to Appellants' Specification "[t]hose of skill will readily appreciate that dose levels can vary as a function of the specific compound, the severity of the symptoms and the susceptibility of the subject to side effects. Preferred dosages for a given compound are readily determinable by those of skill in the art by a variety of means." (Specification 10: ¶ 33).

10. Jiang teaches "that it was known in the art that [the topical] administration of cyclosprorin A [sic], which is 'remarkably similar' in biological properties with FK506, to mice inhibited skin tumor formation in mice" (*id.*; Jiang 67, col. 1, ll. 7-13 and 69, col. 2, ll. 20-22).

11. Jiang "demonstrate tumor inhibition in Figure 1 via FK506 in mice with papillomas promoted by DMBA/TPA treatment . . ." (Answer 3).

12. "A topical application of FK506 to mouse skin 15 min before each TPA treatment resulted in a dose-related inhibition of tumor formation" (Jiang 67: abstract).

13. "Topical application of CsA . . . inhibited various biochemical reactions of skin in response to TPA application. . . ." (Jiang 69, col. 2, ll. 20-22).

14. Flanagan teaches that cyclosporin A and FK506 have similar properties (Answer 4).

15. Bolontrade teaches that "[a]ngiogenesis is an early event in the development of chemically induced skin tumors" (Bolontrade title).

16. Topical application of TPA results in the development of a chemically induced skin tumor (Jiang 67, col. 1, ll. 10-13; Bolontrade 2108, col. 1, ll. 60-64).

DISCUSSION

ANTICIPATION:

Claims 8-11, 15-18, 35, 37, 39, 40, and 44 stand rejected under 35 U.S.C. § 102(b) as anticipated by Jiang.

The Examiner contends that Jiang's method includes "all the steps of the instant methods and use the same compound specifically recited in the claims and the effects [inhibiting angiogenesis/vascular development] are

considered to be inherent in the prior art methods" (Answer 3, alteration original). We disagree.

We understand the Examiner's argument to be that since "[a]ngiogenesis is an early event in the development of chemically induced skin tumors" (Bolontrade title), by inhibiting tumor formation Jiang's method inherently results in the inhibition of angiogenesis/vascular development. The problem with the Examiner's rationale is that the method of claims 8-11, 15-18, 35, 37, 39, 40, and 44 require the *systemic* administration of a Ca2+/calcineurin/NF-ATc inhibitory agent (e.g., FK506). Jiang teaches that *systemic* administration of immunosuppressants, such as FK506 and cyclosporin A, "promotes carcinogenesis in parallel with the suppression of T cell functions" (Jiang 69, col. 2, ll. 49-51). Therefore, the inherency argument relied upon by the Examiner is directly refuted by the express teachings in Jiang. In contrast, Jiang teaches that it is the *topical* administration of FK506 that resulted in the inhibition of tumor formation (Jiang 67: abstract).

For the foregoing reasons we reverse the rejection of claims 8-11, 15-18, 35, 37, 39, 40, and 44 under 35 U.S.C. § 102(b) as anticipated by Jiang.

OBVIOUSNESS:

Claims 36-44, 46, and 47 stand rejected under 35 U.S.C. § 103 as being unpatentable over the combination of Jiang and Flanagan.

According to the Examiner, since the prior art "teaches the interchangeable use of [c]yclosporin A and Fk506 and rapamycin based on their biological properties . . . [a person of ordinary skill in the art at the time

the invention was made would] use compounds with the specific biological properties of cyclosprorin A [sic] and FK506 in the method of Jiang . . . ." (Answer 5.)

CLAIMS 36-44:

Claims 36-44 depend from either claim 8 or claim 15. Accordingly, claims 36-44 require that the Ca2+/calcineurin/NF-ATc inhibitory agent be administered *systemically*. As discussed above, Jiang does not teach the *systemic* administration of either cyclosporin A or FK506.

The Examiner relies on Flanagan to teach that FK506 and cyclosporin have similar properties (Answer 4). The Examiner fails to identify, and we do not find, a portion in Flanagan that teaches the systemic administration of a Ca2+/calcineurin/NF-ATc inhibitory agent (e.g. FK506 or cyclosporin A) to a host. Accordingly, Flanagan fails to make up for the deficiencies in Jiang.

Therefore, we reverse the rejection of claims 36-44 under 35 U.S.C. § 103 as being unpatentable over the combination of Jiang and Flanagan.

CLAIMS 46 and 47:

Claims 46 and 47, however, stand on a different footing. Appellants provide separate arguments for claim 46 and 47. Accordingly, we address each claim below.

CLAIM 46:

Claim 46 is drawn to a method of inhibiting angiogenesis/vascular development in a host, e.g., a mouse. Claim 46 requires the host (mouse) to

have a condition associated with unwanted angiogenesis, e.g., the development of a skin tumor in response to TPA exposure. The method of claim 46 comprises administering (e.g., topically) to the host (mouse) an effective amount of a cyclosporin to inhibit (e.g., prevent from happening) angiogenesis/vascular development in the host (mouse) having a condition associated with the unwanted angiogenesis (e.g., the development of a skin tumor in response to TPA exposure).

Jiang teaches that the topical application of an effective amount of cyclosporin A or FK506 to a mouse suppressed skin tumor promotion caused by exposure to TPA (Jiang 69, col. 2, ll. 18-20 and 23-24; Answer 4). In addition, the Examiner relies on Flanagan to teach that FK506 and cyclosporin A have similar properties. In our opinion, the Examiner has presented the evidence necessary to establish a prima facie case of obviousness.

In response, Appellants assert that Jiang fails to teach (1) that papilloma formation in Jiang's mouse model requires angiogenesis, (2) that the ability of FK506 to inhibit papilloma formation in Jiang's mouse model is due to its anti-angiogenic activity, and (3) that FK506 can inhibit angiogenesis (Br. 15). Appellants assert that Flanagan fails to make up for the deficiencies in Jiang. We are not persuaded by Appellants' arguments. "[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious" the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." *KSR Int'l Co. v. Teleflex Inc.*, 127 Ct. 1727, 1740, 82 USPQ2d 1385, 1396 (2007).

On this record, the evidence relied upon by the Examiner teaches the administration of the same active agent, to the same host, in an amount that suppresses the development of chemically induced skin tumors. While the evidence is silent about the inhibition of angiogenesis/vascular development, it is well recognized that merely discovering and claiming a new benefit of an *old* process cannot render the process again patentable. *In re Woodruff*, 919 F.2d 1575, 1578 16 USPQ2d 1934, 1936 (Fed. Cir. 1990).

For the foregoing reasons we affirm the rejection of claim 46 under 35 U.S.C. § 103 as being unpatentable over the combination of Jiang and Flanagan.

CLAIM 47:

Claim 47 is drawn to a method of inhibiting tumor growth in a host, e.g., a mouse. Claim 47 requires the host (mouse) to have a neoplastic disease condition, e.g., the development of a skin tumor in response to TPA exposure. The method of claim 47 comprises administering (e.g., topically) to the host (mouse) an effective amount of a cyclosporin to inhibit (e.g., prevent from happening) tumor growth in the host (mouse) having a neoplastic disease condition (e.g., the development of a skin tumor in response to TPA exposure).

Jiang teaches that the topical application of an effective amount of cyclosporin A or FK506 to a mouse suppressed skin tumor promotion caused by exposure to TPA (Jiang 69, col. 2, ll. 18-20 and 23-24; Answer 4). In addition, the Examiner relies on Flanagan to teach that FK506 and cyclosporin A have similar properties. In our opinion, the Examiner has

presented the evidence necessary to establish a prima facie case of obviousness.

In response, Appellants assert that Jiang's model is not designed to determine the effect of FK506 on established tumor growth (Br. 16). Instead, Appellants assert that Jiang's studies are designed to determine the ability of an agent to inhibit papilloma formation in a mouse model (*id.*). We are not persuaded by Appellants' argument.

Claim 47 is not drawn to the treatment of "established tumor growth." Instead, claim 47 is drawn to the inhibition of tumor growth in a host having a neoplastic disease condition. According to Appellants' Specification, treatment "includes situations where the pathological condition, or at least symptoms associated therewith, are completely inhibited, *e.g.*[,] prevented from happening . . . ." Jiang teaches that the topical administration of FK506 or cyclosporin A inhibits tumor (papilloma) formation in a mouse model (Jiang 69, col. 2, ll. 18-20 and 23-24; Br. 16).

For the foregoing reasons, we find no error in the rejection of claim 47 under 35 U.S.C. § 103 as being unpatentable over the combination of Jiang and Flanagan. Accordingly, the rejection is affirmed.

CONCLUSION

In summary, we reverse the rejection under 35 U.S.C. § 102(b) and the rejection of claims 36-44 under 35 U.S.C. § 103. We affirm the rejection of claims 46 and 47 under 35 U.S.C. § 103.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED-IN-PART

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